

INTERNET COOPERATION TREA.

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Washington D.C. 20231
United States of America

in its capacity as elected Office

Date of mailing (day/month/year) 16 November 1995 (16.11.95)	
International application No. PCT/IE95/00025	Applicant's or agent's file reference P95-20-PCT
International filing date (day/month/year) 06 April 1995 (06.04.95)	Priority date (day/month/year) 06 April 1994 (06.04.94)
Applicant FREEMAN, Virginia et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
23 October 1995 (23.10.95)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

PATENT COOPERATION TREATY PCT

REC'D	29 APR 1996
PCT	PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P95-20-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/IE 95/ 00025	International filing date (day/month/year) 06/04/1995	Priority date (day/month/year) 06/04/1994
International Patent Classification (IPC) or national classification and IPC A61K9/51		
Applicant ELAN CORPORATION, PLC et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This **REPORT** consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consists of a total of _____ sheets.

3. This report contains indications and corresponding pages relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 23/10/1995	Date of completion of this report 26.04.96
Name and mailing address of the IPEA: European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer B. Merkl Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT**I. Basis of the report**

1. This report has been drawn up on the basis of (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

☒ the international application as originally filed.

☐ the description, pages _____, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☐ the claims, Nos. _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. _____, filed with the letter of _____,
Nos. _____, filed with the letter of _____.

☐ the drawings, sheets/fig _____, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____.
☐ the claims, Nos. _____.
☐ the drawings, sheets/fig _____.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Intern. application No.

PCT/IE95/00025

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 5-16	YES
	Claims 1-4	NO
Inventive Step (IS)	Claims	YES
	Claims 1-16	NO
Industrial Applicability (IA)	Claims 1-16	YES
	Claims	NO

2. CITATIONS AND EXPLANATIONS

1. The following documents have been used for the purposes of this report:

D1 = EP-A-0257310

D2 = EP-A-0145240

D3 = EP-A-0330180

2. D1 discloses an effervescent drug composition comprising the active ingredient microencapsulated in cellulose polymer derivatives. Novelty of the subject-matter of present claims 1-4 cannot be acknowledged as no evidence has been submitted that the cellulose polymer used in D1 is not biodegradable in the sense of the explanation given in the present application on page 7, lines 16-20 and that the drugs cited in the bridging sentence of columns 3 and 4 of D1 do not belong to the classes of medicaments cited in present claim 1-4.

D2 (cited as X-document in the international search report) is not regarded to destroy the novelty of the

present claims as no effervescent formulation is disclosed in D2.

3. D1 is regarded to represent the closest prior art as it differs (if it differs at all, see item 2.) from the subject-matter claimed in present claim 1 only in that other drugs or another polymer is used. D1 discloses almost the same release pattern (compare figures). That means that the problem, namely to achieve a once daily formulation has already been solved by D1. It is not clear what additional problem is to be solved by the present application especially as prolonged release preparations are known from D2 and D3 comprising microcapsules the coating of which consists of biodegradable polymers such a lactic acid polymer. The dependent claims do not appear to contain any features which might render them patentable as said features are normal processing option for the skilled person in the field of pharmaceutical formulations.

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

The requirements of Rule 5.1(a)(ii) PCT have not been met as the documents D1-D3 have not been identified in the description and the relevant background art disclosed therein has not been briefly discussed.

Claim 6 contains all features of Claim 1. Therefore it has to be drafted rather as a claim dependent on claim 1.

Claim 2 is drafted rather as a problem to be solved than the solution expressed in technical terms. The choice of an appropriate pH is obvious for the skilled person (compare e.g. D2, sentence bridging page 10 and page 11).

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

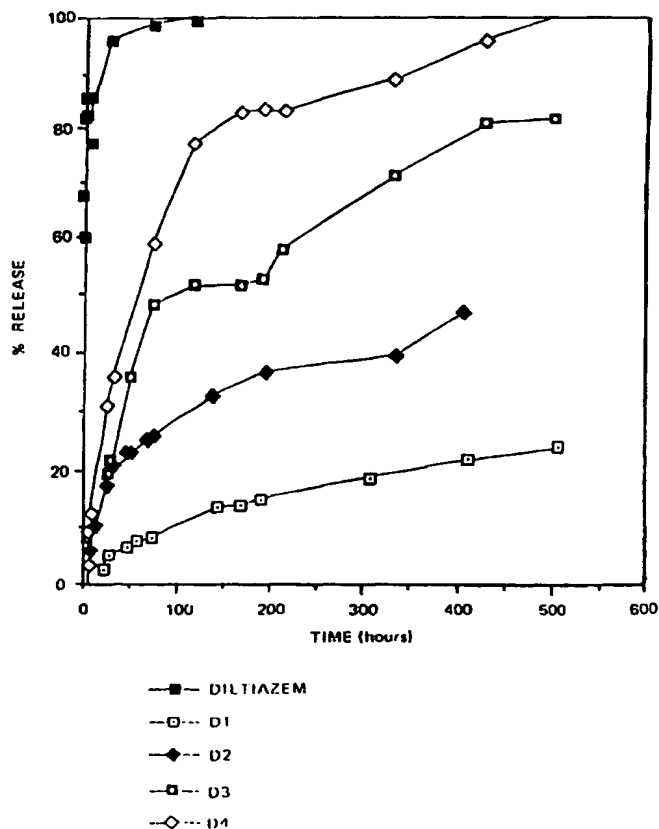
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61K 9/51, 9/52, 9/46, 9/56, 9/58, 9/64		A1	(11) International Publication Number: WO 95/27482
			(43) International Publication Date: 19 October 1995 (19.10.95)
(21) International Application Number: PCT/IE95/00025		(81) Designated States: AU, CA, JP, NZ, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).	
(22) International Filing Date: 6 April 1995 (06.04.95)			
(30) Priority Data: 940292 6 April 1994 (06.04.94) IE		Published With international search report.	
(71) Applicant (for all designated States except US): ELAN CORPORATION, PLC [IE/IE]; Monksland Industrial Estate, Athlone, County Westmeath (IE).			
(72) Inventors; and			
(75) Inventors/Applicants (for US only): FREEMAN, Virginia [IE/IE]; Tarmon, Castlerea, County Roscommon (IE). RAMTOOLA, Zebunnissa [IE/IE]; 163 Charlemont, Griffith Avenue, Dublin 9 (IE).			
(74) Agent: ANNE RYAN & CO.; 60 Northumberland Road, Ballsbridge, Dublin 4 (IE).			

(54) Title: EFFERVESCENT PHARMACEUTICAL FORMULATIONS CONTAINING CONTROLLED RELEASE BIODEGRADABLE MICROCAPSULES

(57) Abstract

Effervescent pharmaceutical formulations for the sustained and controlled oral administration of a drug selected from a calcium channel blocker, an ACE inhibitor, a narcotic analgesic or analogues or combinations thereof, the formulation comprising microcapsules in which the drug is entrapped in a biodegradable polymer, for example poly-L lactide. The pH of the formulation can be varied to optimize the release of the or each drug from the formulation. Microcapsules suitably have a D 50 % between about 100 nm and 900 nm and a drug loading of the order of about 10 % to 70 % by weight. The formulations can be used to administer the drugs to a patient on a once-daily basis so as to achieve a therapeutic effect over a substantially 24-hour period.



INTERNATIONAL SEARCH REPORT

Intern

Application No

PCT/IE 95/00025

A. CLASSIFICATION OF SUBJECT MATTER

A 61 K 9/51, A 61 K 9/52, A 61 K 9/46, A 61 K 9/56,
A 61 K 9/58, A 61 K 9/64

According to International Patent Classification (IPC) or to both national classification and IPC 6

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A 61 K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP, A, 0 257 310 (BIO-DAR LTD.) 02 March 1988 (02.03.88), claims 1,2,4; column 6, lines 50-56; column 3, line 50 - column 4, line 4.	1-3
X	EP, A, 0 145 240 (TAKEDA CHEMICAL INDUSTRIES, LTD.) 19 June 1985 (19.06.85), abstract; claims 1,4-6,10; page 2, lines 13-23; page 6, lines 1-12; page 7, lines 1-3; page 9, lines 10-22; page 10, line 36 - page 11, line 20;	1-3, 5, 9, 10, 12, 13

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search
23 May 1995

Date of mailing of the international search report

03. 07. 95

Name and mailing address of the ISA

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Authorized officer

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT.

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	page 17, lines 1-9. --	
Y	EP, A, 0 330 180 (BIOMATERIALS UNIVERSE, INC.) 30 August 1989 (30.08.89), abstract; claims 1-6; page 3, line 38 - page 4, line 32; page 5, lines 36-51. --	1-10, 12,13, 16
Y	US, A, 5 178 878 (WEHLING F. et al.) 12 January 1993 (12.01.93), claims 1,6; column 2, lines 59-65; column 3, lines 45-48; column 4, lines 56-62; column 5, lines 51-62; column 11, lines 38-50 (cited in the application). --	1-10, 12,13, 16
Y	US, A, 5 133 908 (STAINMESSE S. et al.) 28 July 1992 (28.07.92), abstract; claims 1,2,6,7; column 6, example 4; column 2, line 27 - column 3, line 18; column 3, lines 27-33; column 11, lines 42,43. --	1-10, 12,13
Y	US, A, 4 824 675 (WONG P.S.L. et al.) 25 April 1989 (25.04.89), claims 1,4,7; fig. 2; column 2, line 31 - column 3, line 12; column 12, line 38 - column 13, line 3; column 13, lines 30-49; column 14, lines 38-47; column 14, lines 64,65; column 15, line 67 - column 16, line 9; column 16, line 35 - column 17, line 46. --	1-10, 12,13
A	DE, A, 2 146 174 (MERCK & CO., INC.) 30 March 1972 (30.03.72), claims 1,10,11; page 2, fifth paragraph - page 4, line 3, examples 5,6; example 28. ----	1,3,12

zum internationalen Recherchen-
bericht über die internationale
Patentanmeldung Nr.

to the International Search
Report to the International Patent
Application No.

rapport de recherche inter-
national relatif à la demande de brevet
international n°

PCT/IE 95/00025 SAE 107574

In diesem Anhang sind die Mitglieder
der Patentfamilien der im obenge-
nannten internationalen Recherchenbericht
angeführten Patentedokumente angegeben.
Diese Angaben dienen nur zur Unter-
richtung und erfolgen ohne Gewähr.

This Annex lists the patent family
members relating to the patent documents
cited in the above-mentioned inter-
national search report. The Office is
in no way liable for these particulars
which are given merely for the purpose
of information.

La présente annexe indique les
membres de la famille de brevets
relatifs aux documents de brevets cités
dans le rapport de recherche inter-
national visé ci-dessus. Les renseigne-
ments fournis sont donnés à titre indica-
tif et n'engagent pas la responsabilité
de l'Office.

Im Recherchenbericht angeführtes Patentedokument Patent document cited in search report Document de brevet cité dans le rapport de recherche	Datum der Veröffentlichung Publication date Date de publication	Mitglied(er) der Patentfamilie Patent family member(s) Membre(s) de la famille de brevets	Datum der Veröffentlichung Publication date Date de publication
EP A1 257310	02-03-88	CA A1 1312283	05-01-93
		DE C0 3775858	20-02-92
		EP B1 257310	08-01-92
		JP A2 2072113	12-03-90
		US A 4710384	01-12-87
EP A2 145240	19-06-85	AT E 42197	15-05-89
		CA A1 1233414	01-03-88
		DE C0 3477732	24-05-89
		EP A3 145240	03-07-85
		EP B1 145240	19-04-89
		ES A1 537325	01-04-86
		ES A5 537325	03-05-86
		ES A1 8605983	01-10-86
		GR A 80818	04-03-85
		HK A 37792	17-01-92
		HU A2 37037	28-11-85
		HU B 193910	28-12-87
		IE B 57721	24-03-93
		JP A2 60100516	04-06-85
		JP B4 1057087	04-12-89
		PT A 79450	01-12-84
		PT B 79450	11-12-86
		SG A 1034/91	17-01-92
		US A 4652441	24-03-87
		US A 4711782	08-12-87
		US A 4917893	17-04-90
		US A 5061492	29-10-91
EP A1 330180	30-08-89	DE C0 68904326	25-02-93
		DE T2 68904326	27-05-93
		EP B1 330180	13-01-93
		JP A2 1216918	30-08-89
		US A 5100669	31-03-92
US A 5178878	12-01-93	AU A1 66012790	28-04-91
		AU B2 646232	17-02-94
		EP A1 494972	22-07-92
		EP A4 494972	12-08-92
		JP T2 5500956	25-02-93
		WO A1 9104757	18-04-91
		US A 5223264	29-06-93
		CA AA 2061917	27-08-93
US A 5133908	28-07-92	AT E 84710	15-02-93
		DE C0 68904483	04-03-93
		DE T2 68904483	19-05-93
		EP A1 349428	03-01-90
		EP B1 349428	20-01-93
		ES T3 2054052	01-08-94
		FR A2 2634397	26-01-90
		FR B2 2634397	19-04-91
		JP A2 2149334	07-06-90
		JP B4 6002224	12-01-94
		AT E 74024	15-04-92
		CA A1 1292168	19-11-91
		DE C0 3777796	30-04-92
		EP A1 275796	27-07-88
		EP B1 275796	25-03-92
		ES T3 2031151	01-12-92
		FR A1 2608988	01-07-88
		FR B1 2608988	11-01-91
		JP A2 63240936	06-10-88
		US A 5118528	02-06-92

US A	4824675	25-04-89	AU A1	16517/88	19-01-89
			AU B2	613040	25-07-91
			CA A1	1319071	15-06-93
			DE C0	3871273	25-06-92
			EP A2	300623	25-01-89
			EP A3	300623	22-03-89
			EP B1	300623	20-05-92
			ES T3	2031238	01-12-92
			JF A2	1031710	02-02-89
			US A	4915949	10-04-90
DE A	2146174	30-03-72	AU A1	33178/71	15-03-73
			FR A5	2106566	05-05-72
			FR B1	2106566	18-04-75
			NL A	7112083	20-03-72